

**APPARATUS AND METHOD FOR AGITATING A SAMPLE
DURING IN VITRO TESTING**

FIELD OF THE DISCLOSURE

5 The present invention relates generally to in vitro testing such as dissolution testing of dosage forms, stents, and other carriers of materials having immediate and/or controlled release characteristics. More particularly, the present invention relates to apparatus and methods for providing actuated movement of such carriers of materials during testing, the prevention of evaporation loss during movement, and components adapted for such apparatus and methods.

10 **BACKGROUND OF THE DISCLOSURE**

 In vitro testing methods such as dissolution testing are useful for simulating the conditions under which a substance such as a pharmaceutical formulation is released under controlled conditions into a physiological environment such as a gastrointestinal or vascular
15 environment. The releasing of a sample formulation into appropriate media such as by dissolution facilitates the acquisition of optical signals or other data from which concentration, release rate or other information can be derived for prediction of or correlation with actual, in vivo conditions. Some techniques entail agitation of the sample in media such as by stirring, rotation, or reciprocation.

20 For example, Chapters 711 (Dissolution) and 724 (Extended Release) of the United States Pharmacopoeia (USP) guidelines describe the use of several techniques for performing agitation in test vessels containing a dissolution medium that is usually temperature-regulated. These techniques include the use of a rotating basket (Apparatus 1), a rotating paddle (Apparatus 2), a reciprocating cylinder (Apparatus 3), and a reciprocating holder (Apparatus 7). Each
25 apparatus requires the insertion of a motor-powered shaft into the test vessel. In Apparatus 1, a stainless steel basket with mesh sides is provided to contain a tablet, capsule or other dosage form and is rotated by a stainless steel shaft. In Apparatus 2, a rotating paddle is formed from a blade and shaft. In Apparatus 3, a glass reciprocating cylinder with open, mesh-covered ends is provided to contain a dosage form. The reciprocating cylinder is vertically raised and lowered in
30 a vessel at a prescribed dip rate. The top of the reciprocating cylinder has a perforated cover that is attached to a shaft. An evaporation cap is fitted over the reciprocating cylinder and the container. This cap, however, has air holes and the shaft required for reciprocation extends

through the cap. Hence, the cap cannot fully seal the interior of the container, and an unacceptable loss of solution by evaporation can result. A similar apparatus is described in U.S. Patent No. 5,011,662. Similarly, in Apparatus 7, other types of sample holders attached to shafts, such as nylon net bags, CUPROPHAN[®] material, stainless steel coils, TEFLON[®] disks, and TEFLON[®] cylinders, are vertically reciprocated in vessels for the testing of dosage forms such as tablets and transdermal patches.

As noted, all such systems have historically required the use of a shaft that must be extended into the media container in order to be able to reciprocate, rotate or stir the sample through the media and thereafter removed. Accordingly, a significant amount of evaporation loss often cannot be avoided in these systems. Evaporation loss can reduce the effectiveness of testing procedures entailing agitation. Moreover, shafts are prone to wobble or become misaligned and hence frequently require recalibration or replacement. In addition, the containers employed to hold media have traditionally been sized to accommodate the largest type of sample or sample holder to be tested. In this manner, the same-sized container can be employed in the testing of a wide range of differently sized samples and sample holders. However, when testing relatively small samples, the standardized container size provides an excessively large volume of media through which the sample is reciprocated. As a result, the resolution of data acquired during testing is not optimized for many kinds of samples. Furthermore, conventional testing methods and apparatus are not specifically designed for handling, supporting, and testing newer types of pharmaceutical delivery means such as stents and other carriers of analytical material.

Therefore, a need exists for an apparatus and method for agitating a sample in a container while preventing—i.e., substantially reducing or eliminating—the loss of contents of the container via evaporation or other mechanisms. A need also exists for an apparatus and method for agitating a sample in a container without the requirement of a shaft extending into the container from the ambient environment. A need further exists for an apparatus and method for agitating a sample in a container in which the volume of the container is better tailored to the size of the sample, the sample holder, and/or other items residing in the container. A need further exists for an apparatus and method for handling, supporting, and testing certain types of carriers of drug compounds or other analytical materials.

SUMMARY OF THE DISCLOSURE

According to one embodiment, a device for actuating movement of a sample carrier during in vitro testing comprises a movable component for supporting the sample carrier in a container. The movable component comprises a drivable component actuatable by non-
5 contacting coupling with a driving source.

According to another embodiment, an apparatus for actuating movement of a sample carrier during in vitro testing comprises a container and a movable component. The movable component is disposed in the container for supporting a sample carrier therein and is drivable by
10 non-contacting coupling with a driving source.

According to another embodiment, an apparatus for actuating movement of a sample carrier during in vitro testing comprises a container, a movable component disposed in the container for supporting a sample carrier therein, and a closure member. The closure member seals the container for substantially preventing loss of contents from the container during
15 actuation of the movable component by a driving source.

According to another embodiment, a container is provided for containing an actuatable sample carrier during in vitro testing. The container comprises first and second container sections. The first container section has a first section volume for containing a drivable component drivable by a driving source. The second container section has a second section
20 volume different from the first container volume for containing a sample carrier connected to the drivable component.

According to another embodiment, a closure device is provided for sealing a container. The closure device comprises a body for covering an opening of the container, and a magnet attached to the body for coupling with a sample carrier holder.

According to another embodiment, a support device is provided for supporting a sample carrier. The support device comprises a body, first and second support members, and a coupling member. The first and second support members are attached to the body and are axially spaced for securing a sample carrier between the first and second support members. The coupling member is attached to the body for coupling with a driving source.

According to a method for agitating a sample carrier, a movable component is provided in a container. The movable component supports a sample carrier carrying material releasable into a medium. The movable component is actuated to move in the container by coupling the

movable component with a driving source disposed in non-contacting relation to the movable component.

According to another method for agitating a sample carrier, a movable component that supports a sample carrier is provided in a container comprising first and second container sections having different volumes. The movable component is actuated to move in the container to allow a material provided by the sample carrier to be released into a medium in one of the container sections.

According to a method for manipulating a sample carrier containing releasable material, a closure member is provided and is adapted for sealing an open end of a container. The closure member is coupled with a support device supporting the sample carrier. The coupling between the closure member and the support device enables the sample carrier to be manipulated by handling the closure member without manually contacting the sample carrier.

A method is also provided for securing a sample carrier containing releasable material to a sample carrier holder in preparation for agitating the sample carrier in a container. The sample carrier is mounted to the sample carrier holder such that a first portion of the sample carrier contacts a first support member of the sample carrier holder. A second support member is attached to the sample carrier holder such that the second support member contacts a second portion of the sample carrier.

In some embodiments or methods, non-contacting coupling is accomplished by magnetic coupling. In some embodiments or methods, permanent magnets are employed for this purpose. In other embodiments or methods, one or more electromagnets are employed to enable selective energization and de-energization and therefore selective coupling and decoupling.

In some embodiments or methods, actuation of the movable component is by reciprocation. In other embodiments or methods, actuation is by rotation or spinning.

In some embodiments or methods, a pick-up component disposed in the container can be coupled with the movable component to facilitate handling of the sample carrier. In some embodiments or methods, the pick-up component includes a magnet for magnetic coupling. In some embodiments or methods, the pick-up component is mounted to, attached to, or otherwise integrated with a closure member.

In some embodiments or methods in which a container is provided, the container has an opening at its bottom to provide access into the container for purposes such as conducting fluid to and from the container or using probes or other instruments. A sealing or closure member can

be employed to selectively close the bottom opening. The sealing or closure member can be provided as a fitting for a conduit such as tubing.

Other embodiments and methods comprise one or more of the features or elements recited above.

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BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a cross-sectional elevation view of a sample test apparatus comprising a test vessel unit and an external driving component according to an embodiment disclosed herein;

Figure 2 is an exploded view of the test vessel unit illustrated in Figure 1A;

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Figure 3 is a top plan view of the interior of a test vessel unit and an external driving component according to an embodiment of the present disclosure;

Figure 4 is a front view of a sample test apparatus adapted for operating one or more test vessel units according to another embodiment;

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Figure 5 is a perspective view of a portion of the sample test apparatus illustrated in Figure 4 at which one or more test vessel units can be located;

Figure 6 is a cross-sectional elevation view of a portion of a sample test apparatus according to an embodiment in which one or more test vessel units have stepped profiles; and

Figure 7 is a cross-sectional elevation view of a bottom portion of a test vessel unit according to another embodiment.

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DETAILED DESCRIPTION OF THE DISCLOSURE

In general, terms such as “communicate”, “coupled” and the like (e.g., a first component “communicates with” or “is in communication with” a second component) are used herein to indicate a structural, functional, mechanical, electrical, optical, magnetic, or fluidic relationship between two or more components or elements. As such, the fact that one component is said to communicate or be coupled with or a second component is not intended to exclude the possibility that additional components may be present between, and/or operatively associated or engaged with, the first and second components.

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As used herein, the term “dosage form” generally encompasses any composition or structure that includes a releasable quantity of material that can provide a sample in dissolution testing or other types of testing. The releasable quantity of material can be, for example, a therapeutically active agent such as pharmaceutical drug, chemical, biochemical, or biologically

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active material intended for in vivo delivery by ingestion, injection, insertion, transdermal delivery, surgical implantation, or the like in a human or animal. The releasable material may be soluble, elutable, suspendable, or diffusible in a suitable medium, or mixable with a medium, or otherwise combinable with or transportable to a medium to facilitate analysis of one or more components of the releasable material by any desired means. Non-limiting examples of dosage forms include tablets, capsules, caplets, gel caps, pellets, microspheres, suppositories, pessaries, gels, ointments, oils, creams, and transdermal patches. In addition, a dosage form can include one or more non-active materials used as fillers, excipients, carriers or retainers of the active agent, coloring agents, tagging or marking agents, preservatives, buffers, means for controlling the release rate of the active material, or a combination of two of more of these functions, and/or for other purposes. Generally, a wide variety of dosage forms are available and known to persons skilled in the art.

As used herein, the term “sample carrier” generally encompasses any dosage form or other structure or material capable of carrying a releasable quantity of material. A “sample carrier” can include any dosage delivery mechanism. In addition to dosage forms, another example of a “sample carrier” is a stent or similar type of prosthesis. Some types of stents can function as a drug delivery mechanism in addition to the more conventional function of keeping a blood vessel open. Typically, a stent can include a generally cylindrical or tubular structure that can be surgically implanted in a blood vessel or other lumen, such as by employing a vascular catheter. A common type of stent is constructed by weaving several filaments in helical patterns to form a tubular, braided structure that is deformable and often has shape memory to some degree. The filaments may be metallic or polymeric. Depending on the function of the stent, the filaments may be essentially permanent or degradable over time subsequent to implantation. The stent may be self-expanding or require the use of a balloon for expansion. The stent can be of the type that is coated with or otherwise carries a releasable material that can be released from the stent at a controlled rate via elution, diffusion, or other mechanism of transport. Generally, a wide variety of stents are available and known to persons skilled in the art.

In addition to dosage forms and stents, other non-limiting examples of “sample carriers” include implantable (bio)(chemo)sensors such as glucose sensors, infusion catheters, dental implants, neurostimulation leads, and spinal repair devices, as these terms are understood by persons skilled in the art.

As used herein, the term “medium” or “media” generally encompasses a solvent such as water, alcohol, and/or any other medium into which a releasable material can be released, as well as any additives or reagents. Often, the medium is buffered at a desired pH level or formulated to emulate a physiological environment such as a gastrointestinal environment or a luminal or coronary environment such as a blood vessel. The term “medium” or “media” can also include materials released from a dosage form, stent or the like, for example a therapeutically active agent, excipient, release rate modifier, and the like. Thus, the term “medium” or “media” can encompass a multi-component combination or matrix such as can be produced in a test vessel, including a solution, suspension, emulsion, particulate-laden mixture, colloidal mixture, or the like.

Examples of embodiments of the subject matter disclosed herein will now be described in more detail with reference to Figures 1-7.

Figure 1 illustrates a sample testing apparatus according to one embodiment, generally designated **10**. Sample testing apparatus **10** can be employed to cause, facilitate, or provide an environment for the release of releasable materials such as therapeutically active agents or other sample analytes of interest from one or more sample carriers **14** into a suitable medium **16**. Sample testing apparatus **10** can be utilized in preparation for or in conjunction with measuring a property or quality relating to the performance of sample carrier **14** or of the releasable material, such as the rate at which an analyte is released from sample carrier **14** over a designated time period. Sample testing apparatus **10** can comprise one or more test vessel units, generally designated **20**; and one or more non-contact driving sources or components, generally designated **100**. Test vessel unit **20** can comprise a container or test vessel **30**; a closure member or device, generally designated **40**; and a non-contact movable component or device, generally designated **60**, which is drivable by non-contact driving component **100**. The term “non-contact” or “non-contacting” means that driving component **100** interacts with movable component **60** in a manner that does not require physical contact between these components, as described by way of example more fully below.

Container **30** can comprise, for example, a tube or vial that typically includes a closed bottom **32** and an opening **34** at its top (Figure 2). Bottom **32** can be hemispherical or rounded as shown in Figure 1, or generally flat as shown in Figure 6. Generally, container **30** can be any structure useful for containing one or more sample carriers **14** and a medium **16** into which one or more materials provided by sample carrier **14** can be released. Preferably, container **30** is

constructed from an inert material, i.e., a material that does not sorb, react or interfere with the analyte being tested. Typically, container 30 is constructed from glass or other material that is transparent or translucent to enable visual access into the interior of container 30. In addition, the material of container 30 is preferably capable of transferring heat in a case where temperature regulation of media 16 in container 30 is desired. In addition, the glass or other material is preferably one that can be manufactured to industry-accepted, repeatable tolerances.

Closure member 40 can comprise any structure that functions to seal opening 34 (Figure 2) and thereby completely or at least substantially prevent the loss of media 16 or other contents from container 30 during the course of a testing procedure. In particular, closure member 40 prevents or at least significantly reduces the escape of evaporated media 16 from container 30, especially under pressurized conditions such as can occur when the contents of container 30 are being heated. In advantageous embodiments, closure member 40, or at least those portions of closure member 40 in contact with container 30, is constructed from a resilient material such as rubber, polyethylene, or other suitable polymer, or a metallic material, to provide an effective seal. Generally, closure member 40 can be a stopper, septum, plug, cap, or any other structure sufficient to cover opening 34 (Figure 2) of container 30 and thereby isolate the interior of container 30 from the ambient environment. In the illustrated embodiment, closure member 40 includes a main portion or body 44 and a central portion or body 48 extending from the main body 44. Main body 44 covers opening 34 and the contact between main body 44 and container 30 may contribute to the sealing of container 30. Main body 44 can be constructed from a rigid material such as DELRIN[®] or a resilient material.

In the exemplary embodiment illustrated in Figure 1, central portion 48 of closure member 40 extends into container 30. One or more surfaces of central portion 48 contact container 30 to form the seal, and thus one or more portions of central portion 48 are advantageously constructed from a resilient material such as polyethylene. In some embodiments, central portion 48 includes one or more annular ribs 48A and 48B that serve as the surfaces sealingly contacting the inside of container 30. The diameter of each rib 48A and 48B can be sized larger than the diameter of an inside surface 36A of container 30 to create an effective sealing interface with container 30 upon insertion of central portion 48 therein. In other embodiments, an outer lateral surface 48C of central portion 48 can be sized to tightly abut against inside surface 36A of container 30 to effect the seal. In still other embodiments, main

body 44 or central portion 48 can include an extended portion (not shown) configured to sealingly fit against an outer surface 36B of container 30 in a similar manner.

Movable component 60 can be disposed in the interior of container 30 as illustrated in Figure 1. Movable component 60 can comprise any structure or device suitable for supporting, holding, or retaining one or more sample carriers 14, and which is capable of being driven to reciprocate, rotate or otherwise move within container 30 without breaking the sealed state of container 30. For example, movable component 60 can be configured to be actuatable by a driving component 100 that is disposed in non-contacting relation to movable component 60. For these purposes, movable component 60 can comprise a sample carrier holder or support member, generally designated 64; and a drivable component, generally designated 90, attached to or integrated with sample carrier support member 64. In some embodiments, movable component 60 can generally be considered as including a body or structure, which advantageously is elongated in the axial direction. The body or structure of movable component 60 can include one or more portions or sections. Sample carrier support member 64 and drivable component 90 are attached to or, equivalently, integrated with or form a part of, the body or structure of movable component 60 or one or more of its constituent portions or sections. In some embodiments as illustrated in Figure 1, the body or structure of movable component 60 can include a portion or section 78 and a portion or section 82.

As indicated previously, sample carrier 14 can comprise any dosage delivery mechanism—that is, any dosage form or other structure or material capable of carrying a releasable quantity of material such as a drug formulation that can be released from sample carrier 14 when subjected to a solvent or other suitable medium 16. Likewise, the structure of sample carrier support member 64 may depend on the type of sample carrier 14 utilized in sample testing apparatus 10. By way of example only and not as a limitation on the scope of the subject matter disclosed herein, Figures 1 and 2 illustrate a sample carrier 14 provided in the form of a stent. Accordingly, sample carrier support member 64 in this example is structured to serve as a stent holder. In other embodiments, sample carrier support member 64 can comprise a basket, disk, netting, cell, cylinder, or the like as needed for supporting or containing other types of sample carriers 14 (e.g., tablets, transdermal patches, etc.) during reciprocation through media 16.

To secure sample carrier 14 to sample carrier support member 64 in a stable manner, sample carrier support member 64 in the present embodiment includes a first support member 72

and a second support member 74 between which sample carrier 14 is mounted. First and second support members 72 and 74 include respective first and second inward-facing surfaces 72A and 74A—i.e., surfaces that face each other and sample carrier 14—against which opposite ends of sample carrier 14 respectively contact or abut. In some embodiments, first and second inward-facing surfaces 72A and 74A are each generally cone-shaped or otherwise angled or tapered relative to the longitudinal axis of container 30 to accommodate sample carriers 14 of different diameters. In some embodiments, first support member 72 is attached to a structure of movable component 60 such as portion 78 that can serve as an axial extension or spacer member between sample carrier support member 64 and drivable component 90.

First and second support members 72 and 74 can be kept spaced apart from and aligned with each other by providing a support rod or portion 82 interconnected between them. First and second support members 72 and 74 can include respective bores 72B and 74B into which the opposing ends of support rod 82 extend. As can be seen in Figure 2, support rod 82 can be made removably attachable to first support member 72, or to another component of sample carrier support member 64 such as spacer member 78, to facilitate the mounting of sample carrier 14 to sample carrier support member 64 and the subsequent removal therefrom. As shown in Figure 1, the removable attachment can be accomplished by any means, such as by providing external threads on support rod 82 for engaging with internal threads formed in a bore 78A of spacer member 78 or bore 72B of first support member 72 that is axially aligned with bore 78A of spacer member 78. Sample carrier 14 is secured to sample carrier support member 64 by placing sample carrier 14 around the length of support rod 82, and inserting the free end of support rod 82 into bore 72B of first support member 72, or through bore 72B and into bore 78A of spacer member 78. Depending on which bores 78A or 72B are threaded, the securing of sample carrier 14 is completed by screwing or inserting the free end of support rod 82 into bore 78A or 72B. The free end of support rod 82 is screwed or inserted far enough into bore 78A and/or 72B to ensure that sample carrier 14 snugly abuts both first and second support members 72 and 74.

Alternatively, support rod 82 can be removably attached to second support member 74 in a similar manner, in which case second support member 74 can be removed from support rod 82 during loading or removal of sample carrier 14. The removability of first support member 72 and/or second support member 74 from support rod 82 also facilitates cleaning or replacement of these individual components.

It will be understood that the subject matter of the present disclosure is not limited to the use of threaded features as the fastening and adjustment means. As an alternative, for example, support rod 82 can be secured to first support member 72 and/or spacer member 78 by press-fitting.

5 As an advantage provided by any of these alternatives, support rod 82 is movable through bore 72B of first support member 72 and bore 78A of spacer member 78. Hence, the position of first support member 72 and/or second support member 74 is adjustable relative to the length of support rod 82 and thus relative to each other. This adjustability or variability in spacing enables sample carrier support member 64 to accept stents or other types of sample carriers 14 of
10 different dimensions. In addition, it can be seen from Figure 1 that sample carrier support member 64 secures sample carrier 14 with minimum contact, and maintains sample carrier 14 centered or substantially centered about the central longitudinal axis of container 30. This configuration avoids rubbing or impact between sample carrier 14 and sample carrier support member 64, and between sample carrier 14 and container 30, thereby enhancing the accuracy of
15 in vitro dissolution testing.

It can be appreciated that the utility and advantages provided by sample carrier support member 64 can extend to a wide variety of sample carriers 14 and lab procedures. Accordingly, sample carrier support member 64 can be employed not only in conjunction with actuation in a non-contact manner such as described herein, but also in conjunction with actuation entailing a
20 direct mechanical linkage with a driving source. Thus, the present disclosure encompasses embodiments and methods in which sample carrier support member 64 is employed with or without non-contact actuation. For example, sample carrier support member 64 can be adapted for direct mechanical reference to a shaft that communicates with a motorized drive assembly, such as when the use of a fully sealing closure member 40 is not desired or required.

25 Drivable component 90 can be any structure capable of being driven to reciprocate and/or rotate within container 30 without physically contacting or engaging the driving source so as not to defeat the sealed state of container 30. One advantage of providing a non-contact drivable component 90 is that the driving source can operate externally relative to container 30. In this manner, the ability of test vessel unit 20 to prevent evaporation or other material loss is fully
30 coextensive with its ability to actuate movement or agitation by reciprocation, rotation, etc. In the illustrated embodiment, non-contact actuation is realized by providing a drivable component 90 that comprises an internal magnetic coupling component. The internal magnetic coupling

component includes an internal magnet 92. Internal magnet 92 can be secured to or integrated with movable component 60 by any means that enables sample carrier support member 64 to be reciprocated or rotated with internal magnet 92 in response to a non-contacting driving input such as the operation of driving component 100. In the embodiment illustrated in Figure 1, for example, drivable component 90 comprises a cap or housing 94 attached to spacer member 78 to enclose internal magnet 92.

Driving component 100 can be any structure capable of causing agitation in container 30 without needing to physically contact or engage any part of movable component 60, and consequently without impairing the sealed state of container 30 and contributing to evaporation losses. Driving component 100 can be positioned externally relative to container 30, and is movable independently from container 30. In advantageous embodiments as illustrated in Figure 1, driving component 100 comprises an external magnetic coupling component. The external magnetic coupling component includes one or more external magnets 102 as needed to establish a magnetic field pattern suitable for maintaining an attraction between external magnet 102 and internal magnet 92 of drivable component 90 across the thickness of the wall of container 30. Driving component 100 can further comprise a support member 104 such as a housing, plate, or the like for supporting external magnet(s) 102. As can be appreciated by persons skilled in the art, the structure of driving component 100 and its proximity to container 30 is such that external magnet 102 is magnetically coupled with internal magnet 92 of drivable component 90 to a degree that enables drivable component 90 to move in response to movement of driving component 100, while preventing drivable component 90 from being decoupled and allowing movable component 60 to drop to the bottom 32 of container 30.

In advantageous embodiments as shown in Figure 3, driving component 100 can comprise a plurality of external magnets 102A, 102B, and 102C circumferentially arranged relative to internal magnet 92. For instance, Figure 3 illustrates three external magnets 102A, 102B, and 102C circumferentially spaced apart at 120 degree intervals, although more or less external magnets 102A, 102B, and 102C at greater or lesser intervals could be employed. External magnets 102A, 102B, and 102C are disposed in respective recesses or pockets 104A, 104B, and 104C formed in support member 104. The arrangement provides a balance of magnetic forces during agitation that can enhance the stability of the coupling relation between internal magnet 92 and external magnets 102A, 102B, and 102C and reduce any skipping, jittering or other undesired motion of movable component 60 (Figures 1 and 2) due to friction or

field imperfections. In this embodiment, container **30** extends coaxially through an aperture **104D** defined by support member **104**, facilitating the ability of external magnet or magnets **102A**, **102B**, and **102C** to maintain a controllable magnetic coupling relation with internal magnet **92**. In other embodiments, driving component **100** can be situated proximate to container **30** without completely circumscribing it.

Figure 3 illustrates a single test site where one container **30** and a set of one or more external magnets **102A**, **102B**, and **102C** are located. In other embodiments, more than one test vessel **20** (Figures 1 and 2) can be operated simultaneously. Hence, a single driving component **100** can be constructed to accommodate several test sites at which respective containers **30** and one or more external magnets or sets of magnets **102A**, **102B**, and **102C** are located. Alternatively, a plurality of driving components **100** can be provided for a corresponding number of test vessel sites. In the case where a plurality of test sites are provided, Figure 3 can be considered as illustrating a section of driving component **100** at which one test site is defined or one of several driving components **100**.

As indicated by arrow **A** in Figure 1, driving component **100** in some embodiments is reciprocable relative to container **30**. In the illustrated embodiment, driving component **100** is axially reciprocable along a length of container **30** although other paths of reciprocation could be rendered. Driving component **100** can be reciprocated by any suitable means, such as a motor and linkage or transmission assembly operatively communicating with driving component **100**. Due to the magnetic coupling between external magnet **102** of driving component **100** and internal magnet **92** of drivable component **90**, the reciprocation of driving component **100** results in reciprocation of movable component **60** as indicated by arrow **B**, including drivable component **90** and sample carrier support member **64**. Consequently, sample carrier **14** and the sample material it carries are reciprocated through media **16** in container **30**.

In the embodiments just described, reciprocation of sample carrier **14** is attained by moving driving component **100** while container **30** remains stationary. An alternative embodiment, however, can be readily appreciated from Figure 1 in which external magnet **102** remains stationary and container **30** is reciprocated. In this alternative embodiment, a suitable driving source is mechanically coupled to container **30** by any known means to cause reciprocative displacement of container **30** through space. Due to the magnetic coupling between external magnet **102** and internal magnet **92**, the position of sample carrier support member **64** and sample carrier **14** relative to the container **30** remains fixed or substantially fixed

while container 30 is being reciprocated. This alternative arrangement could be provided to yield an analogous hydrodynamic effect within container 30, in which the position of sample carrier 14 changes relative to the volume of media 16 residing in container 30.

In advantageous embodiments, as illustrated in Figure 1, sample testing apparatus 10 further comprises a pick-up component 110 disposed in container 30 for selective coupling or engagement with movable component 60. Pick-up component 110 facilitates removal of movable component 60 and any sample carrier 14 supported thereby from container 30, and enables sample carrier 14 to be handled or transported without contact to reduce the risk of contamination or damage. In advantageous embodiments, pick-up component 110 is attached to or, equivalently, integrated with closure member 40. By this configuration, after movable component 60 has been coupled with or attached to pick-up component 110, movable component 60 and sample carrier 14 can be removed from container 30 by removing closure member 40. For embodiments in which drivable component 90 comprises an internal magnetic coupling, pick-up component 110 can comprise a pick-up magnet 112. As illustrated in Figure 1, pick-up magnet 112 can be enclosed within central portion 48 of closure member 40. Pick-up magnet 112 can be configured (e.g., size, material, or the like) to induce a stronger magnetic coupling relation with drivable component 90 as compared with driving component 100. In this manner, when it is desired to remove movable component 60 and sample carrier 14 from container 30, driving component 100 is actuated to translate movable component 60 toward pick-up component 110—i.e., in the direction of opening 34 (Figure 2) of container 30—by a greater stroke than normally occurs during the afore-described reciprocative cycle. The distance between internal magnet 92 of movable component 60 and pick-up magnet 112 reduces to a value at which the magnetic attraction between internal magnet 92 and pick-up magnet 112 is stronger than that between internal magnet 92 and external magnet 102 of driving component 100, at which time closure member 40 can be manipulated to remove movable component 60 from container 30.

As schematically indicated in Figure 1, driving component 100 can be powered by a drive system 120 of any type envisioned by persons skilled in the art. Generally, drive system 120 can comprise any system or assembly capable of producing reciprocative and/or rotative (including stirring) motion that can be transferred to drivable component 90 via the non-contact coupling provided by driving component 100. Thus, drive system 120 can include a motor and a transmission or linkage (not shown) communicating with driving component 100. Depending on

the design of drive system **120**, driving component **100** may be considered as being a part of the transmission or linkage. Reciprocative and/or rotative motion can be produced by a reversible motor, i.e., one whose rotational direction can be repeatedly changed, or by a transmission or linkage designed to convert motor-generated rotation into reciprocation and/or rotation. For instance, drive system **120** can comprise a DC motor coupled to a crank mechanism that produces linear reciprocating motion. Other non-limiting examples of transmission or linkage components through which driving component **100** can communicate with a motor include rack and pinion arrangements, belt or chain and pulley arrangements, carriages or stages guided by tracks, or the like. As a general matter, a wide variety of drive systems **120** are known to persons skilled in fields such as lab automation and robotics, and accordingly drive system **120** need not be described further in the present disclosure.

In operation, test vessel **20** is prepared by assembling movable component **60** with sample carrier **14** including the sample to be tested, as previously described with reference to Figure 2. Container **30** is filled to a desired level with a selected medium **16**. Movable component **60** is then inserted into container **30** and closure member **40** is used to seal container **30**. If pick-up component **110** is provided and integrated with closure member **40**, closure member **40** can be handled to insert movable component **60** into container **30**. Before, during or after assembly, test vessel **20** is mounted at a suitable test site where driving component **100** can be actuated. Actuation of driving component **100** causes movement of movable component **60**, and thus sample carrier **14** and the sample material carried thereby, by way of reciprocation or rotation through medium **16** residing in container **30**. In processes where sealing is desired, container **30** remains sealed during agitation to prevent the loss of any contents of container **30**.

It can be appreciated that the utility and advantages provided by effecting movement or agitation in container **30** by means of non-contact actuation can extend to implementations in which the use of a fully sealing closure member **40** is not desired or required. It will therefore be understood that the present disclosure encompasses embodiments and methods in which non-contact actuation is enabled without sealing container **30** in the manner described herein.

Referring now to Figure 4, a sample testing apparatus, generally designated **200**, is illustrated according to another embodiment in which several testing procedures can be respectively performed in a plurality of test vessel units **20** operating simultaneously. Sample testing apparatus **200** can include a frame, generally designated **202**, for supporting various components. In some embodiments, sample testing apparatus **200** includes a vessel support

assembly, generally designated **210**. Vessel support assembly **210** can comprise any structure suitable for defining an array of test sites at which one or more test vessel units **20** can be located—preferably in a consistent, repeatable manner—and which is compatible with the use of a drive system **120** and one or more driving components **100** as described above. For example, vessel support assembly **210** can comprise one or more vessel plates. In the exemplary embodiment best illustrated in Figure 5, vessel support assembly **210** comprises a top vessel plate **222** having apertures **222A** through which test vessel units **20** can be extended. Vessel support assembly **210** also comprises a medial vessel plate **224** disposed below top vessel plate **222**, which also has apertures **224A** for positioning test vessel units **20**, as well as a base plate **226** for supporting bottom **32** of each test vessel unit **20** mounted in vessel support assembly **210**.

As shown in Figure 4, frame **202** of sample testing apparatus **200** can support a temperature regulating section **230** at which vessel support assembly **210** and test vessel units **20** are located. Temperature regulating section **230** can comprise any structure suitable for regulating the temperature of the media contained in test vessel units **20** if desired, such as when proceeding in accordance with certain published USP guidelines. For example, temperature regulating section **230** can comprise a temperature-controlled water bath in which test vessel units **20** are immersed. Alternatively, means can be provided for heating individual test vessel units **20** directly instead of providing a bath. Techniques for regulating temperature during dissolution testing are generally known to persons skilled in the art.

As also illustrated in Figure 4, sample testing apparatus **200** can comprise a control head assembly **240** supported by frame **202** above vessel support assembly **210**. In general, control head assembly **240** can provide any number of functions that enable automation or control of one or more aspects of testing procedures, including user input, readout, and interfacing with other modules of a larger analytical system. Control head assembly **240** can also be used to contain a drive system **120** such as previously generally described.

In advantageous embodiments, a single drive system **120** enables the agitation of samples in all test vessel units **20** operating in sample testing apparatus **200**. As shown in Figure 4, a linkage assembly, generally designated **250**, serves as the interface between drive system **120** and driving component **100**. Generally, linkage assembly **250** can include any suitable arrangement of one or more rods, pistons, or other linkage members **252** as needed to realize this interface. As illustrated in Figure 5, one or more linkage members **252** may be connected to

support member **104** of driving component **100**. In reciprocating embodiments, reciprocation of one or more linkage members **252** as indicated by arrow **C** results in reciprocation of external driving component **100** as indicated by arrow **D**.

As also shown in Figures 4 and 5, driving component **100** can comprise a single support member **104** such as an agitation platform. Support member **104** can be configured for a plurality of test sites as previously described in conjunction with Figure 3 to provide one or more external magnets (e.g., external magnets **102A**, **102B**, and **102C** in Figure 3) for each corresponding test vessel unit **20**. As shown in Figure 5, the apertures **104A** of support member **104** are coaxially aligned with those of vessel plates **222** and **224** to enable a single support member **104** to reciprocate generally in parallel with the axes of test vessel units **20**. In other embodiments, test vessel units **20** can be associated with separate respective driving components **100**, with each driving component **100** including an external magnet **102** or set of external magnets **102A**, **102B**, and **102C**.

In operation, one or more test vessel units **20** are prepared and assembled as previously described, and test vessel units **20** are loaded into vessel support assembly **210**. Drive system **120** is operated to reciprocate driving component(s) **100**. Each external magnet **102** (Figure 1) or set of external magnets **102A**, **102B**, and **102C** (Figure 3) reciprocates with support member **104** of driving component **100**. Accordingly, for every test vessel unit **20** being operated that contains a movable component **60** (Figures 1 and 2) as described above, the reciprocation of driving component **100** drives movable components **60** to likewise reciprocate within test vessel units **20** (as indicated by arrow **B** in Figure 1), thereby simultaneously agitating all corresponding sample carriers **14**. In preparation for removing sample carriers **14** from their respective containers **30**, drive system **120** can be operated or programmed to actuate driving component **100** upwardly to bring each movable component **60** into coupling relation with respective pick-up components **110** (Figure 1), as described above according to embodiments of the present disclosure.

In an alternative embodiment in which external magnets **102** (Figure 1) are fixed in position while test vessel units **20** themselves are reciprocated, one of the plates of vessel support assembly **210** could be provided with means for engaging test vessel units **20** and coupled with linkage assembly **250** in an analogous manner.

Figure 6 illustrates another embodiment, generally designated **300**, in which sample testing can be optimized for a wide range of sizes of sample carriers **14**. A test vessel, generally

designated **320**, comprises a container **330** having a necked-down or stepped-down profile.

Container **330** includes at least two distinct first and second container sections **330A** and **330B**.

First and second container sections **330A** and **330B** have different axial lengths and/or inside

diameters, and thus have different internal volumes. Typically, the media used in container **330**

will occupy only second container section **330B**. Sample carrier **14** is mounted to sample carrier support member **64** of movable component **60** such that sample carrier **14** is agitated only

through second container section **330B** where the medium is located. Second container section

330B is sized to provide the optimal media volume for the particular sample carrier **14** being

tested. In the context of dissolution testing, the optimal media volume is that which yields the

highest resolution in the course of acquiring the optical data utilized to generate a dissolution

curve. Typically, the optimal media volume is the smallest volume feasible for testing a sample carrier **14** of a given size.

Figure 6 also illustrates another test vessel, generally designated **420**, comprising a

container **430** that likewise includes first and second container sections **430A** and **430B** of

different volumes. By comparison, second container section **430B** of container **430** is larger

than second container section **330B** of container **330** in order to accommodate, or optimize test

conditions for, a larger-sized sample carrier **14**. However, in order to standardize the sizes and

features of as many other components as possible (e.g., closure member **40**, drivable component **90**, driving component **100**, vessel support assembly **210**, and the like), the dimensions of first

container section **430A** of container **430** can be made the same as those of first container section

330A of container **330**. Thus, both test vessel **420** and test vessel **320** can operate in the same

apparatus with minimal or no modifications or adjustments.

As described previously, the movement of movable component **60** can constitute a linear

reciprocation along the longitudinal axis of container **30** and/or rotation about the longitudinal

axis, depending on what mode of agitation is appropriate or desired for the test being conducted.

Referring to Figure 3, in some embodiments, rotation of movable component **60** can be

magnetically actuated by rotating external magnet(s) **102A**, **102B**, **102C** to cause internal magnet

92 to rotate by means of the resulting changes in orientation of the magnetic field. As indicated

by arrow **E** in Figure 3, the rotation can be in one direction through repeating full (360-degree)

cycles or can be in alternating directions (e.g., clockwise/counterclockwise) through partial cycles.

The rotation of external magnet(s) **102A**, **102B**, **102C** can be actuated and controlled by any suitable driving means now known or later developed. Without intending to limit the scope of the subject matter in any way, one example of a driving means includes an annular rotatable member (not shown) coaxially disposed about container **30** (Figure 3) and supported by support member **104** of driving component **100**. External magnet(s) **102A**, **102B**, **102C** are mounted to and rotate with the rotatable member. The rotatable member can include pulley- or cog-like features to be driven by a belt or chain. Alternatively, the rotatable member can include teeth for meshing with a driving gear coupled with driving system **120** (Figures 1 and 4).

Referring now to Figure 7, another embodiment is disclosed in which container **30** (or container **330** or **430** shown in Figure 6) has an opening **502** at its bottom **32**. Bottom opening **502** can serve a number of functions, particularly as an inlet and/or outlet for liquid or instruments before, during, and after dissolution of sample material. For example, bottom opening **502** can be employed to fill container **30** with media **16** (Figure 1), take samples from container **30**, provide access for a temperature probe, admit rinsing fluid into container **30** for washing, admit buffers or reagents into container **30**, refill or replenish media **16**, provide access for an optical probe or light pipe to acquire optical-based data, and so on. For these and any other such purposes, bottom opening **502** can be selectively opened and closed by fitting a closure member **504** into sealing contact with the edge-area surfaces defining bottom opening **502**. Alternatively, closure member **504** can be formed as a fitting with a bore adapted to receive a lab-quality conduit **506** suitable for handling fluid. Conduit **506** may be removable such as by fashioning closure member **504** with a Luer-type fitting, or may be attached to closure member **504** by a suitable bonding material such as epoxy resin. As appreciated by persons skilled in the art, conduit **506** can be part of a closed fluidic system and thus does not detrimentally affect the ability of closure member **40** to completely seal container **30** during desired time periods.

The functions of or activities enabled by bottom opening **502** are traditionally carried out from the top of container **30**. Indeed, the afore-described closure member **40** (Figure 1) that is fitted to top opening **34** in some embodiments could be provided with one or more conduits, probes and the like, and such an embodiment is encompassed within the scope of the present disclosure. However, the use of bottom opening **502** in the present embodiment allows closure member **40**, when provided, to be optimized for its primary purpose of preventing evaporation loss.

In any of the embodiments described herein in which magnets are employed to enable movement by non-contacting actuation, it will be understood that the magnets can include permanent magnets, electromagnets, or both. Accordingly, terms such as “magnet”, “magnetic” and “magnetic coupling” as used throughout this disclosure encompass the use of a permanent magnet and/or an electromagnet. Stated alternatively, the term “magnet” as used herein can be a material that exhibits magnetization due to its possessing a permanent magnetic dipole or in response to an external field or application of electrical current. For instance, external magnets **102A, 102B, 102C** (Figure 3) and/or pick-up magnet **112** (Figure 1) can be provided as electromagnets to enable selective magnetic coupling with internal magnet **92** (Figure 1). In embodiments in which an electromagnet is provided, it will be appreciated by persons skilled in the art that the electromagnet can be placed in communication with a suitable electrical current or voltage source through electrical leads, and may entail the use of coils, solenoids, or the like to produce a magnetic field of sufficient strength to control, for example, movable component **60**.

The use of electromagnets can offer functional advantages. For instance, if provided as an electromagnet, pick-up magnet **112** can be energized only when it is desired to use closure member **40** to install or remove movable component **60** and de-energized at other times. After movable component **60** has been installed in container **30**, movable component **60** can be decoupled from pick-up magnet **112** by de-energizing pick-up magnet **112** such as by cutting off electrical current to pick-up magnet **112**. This allows movable component **60** to drop farther into container **30** to a suitable operating position at which movable component **60** can be magnetically coupled with external magnet(s) **102A, 102B, 102C**, either due to an electrical current applied to external magnet(s) **102A, 102B, 102C** or to the presence of a permanent magnetic dipole in the material of external magnet(s) **102A, 102B, 102C**. In addition, the magnetic coupling between external magnet(s) **102A, 102B, 102C** and movable component **60** can be selectively established in the case where external magnet(s) **102A, 102B, 102C** are electromagnets.

It will be understood that various aspects or details of the invention may be changed without departing from the scope of the invention. Furthermore, the foregoing description is for the purpose of illustration only, and not for the purpose of limitation—the invention being defined by the claims.